UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/454,711	12/06/1999	JOHANNES B. M. M. VAN BREE	16994-012710	4156

30095 7590 12/17/2001

GENZYME CORPORATION C/O TOWNSEND AND TOWNSEND AND CREW
TOWNSEND AND TOWNSEND & CREW, LLP
TWO EMBARCADERO CENTER, 8TH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
PRATS, FRANCISCO CHANDLER	
ART UNIT	**PAPER NUMBER**
1651	14

DATE MAILED: 12/17/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/454,711	Applicant(s) VAN BREE ET AL.	
	Examiner Francisco C Prats	Art Unit 1651	/

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11 and 14-38* is/are pending in the application.

4a) Of the above claim(s) *27-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-11, 14-26 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendment filed October 15, 2001, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 2, 12 and 13 have been cancelled.

Claims 35-38 have been added.

Claims 1, 3-11 and 14-38 are pending.

Election/Restrictions

Claims 27-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7, filed March 5, 2001.

Claims 1, 3-11, 14-26 and 35-38 are examined on the merits.

Claim Rejections - 35 USC § 103

Claims 1, 3-11, 14-26 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kikuchi et al (J. Clin. Invest. 101(4):827-833 (1998)), de Barsy et al (Birth Defects, Original Article Series, Vol. IX, No.2, pages 184-190 (1973)), and Reuser et al (U.S. Pat. 6,118,045) in view of Bijvoet et al

(Biochim. Biophys. Acta 1308:93-96 (1996)) and Van Hove et al (Biochem. Mol. Biol Int'l. 43(3):613-623 (1997)).

As amended, the claims recite the treatment of infantile Pompe's disease wherein at least 10 mg/kg body weight per week of human acid α-glucosidase are administered to a patient which survives at least to one year of age. As discussed in the previous office action, each of Kikuchi, de Barsy and Reuser suggest the treatment of Pompe's disease by administering human acid α-glucosidase to patients in need thereof. Kikuchi, deBarsy and Reuser differ from the claims in that the dosage amounts disclosed therein are smaller than those recited in various embodiments recited in applicant's claims, and that the dosages are not gradually increased as recited in some other embodiments in the claims.

However, de Barsy notes that the lack of significant clinical effects was likely due to the small amount of enzyme administered owing to lack of availability, and that the efforts disclosed therein must be considered preliminary. *See* p. 189, col. 1. Thus, de Barsy clearly suggests that increased dosage would be desirable in treating the disease. Moreover, each of Reuser (claims 18-20), Bijvoet (abstract at page 94, disclosing *in vitro* internalization of enzyme) and Van Hove (sentence spanning pages 613 and 614, disclosing endocytosis of 110 kD

form of the enzyme and delivery to liver and heart upon injection) clearly suggest that relatively large amounts of the enzyme are obtained by the methods disclosed therein, and that the enzymes prepared therein are suitably targeted to the desired tissues, including muscle.

Thus, the artisan of ordinary skill, recognizing from de Barsy that high dosages would have been reasonably expected to improve the results disclosed therein, would have been motivated to have increased the enzyme dosage to the amounts recited in applicant's claims, suitable quantities of the enzymes being made available by the techniques disclosed in the Reuser, Bijvoet and Van Hove disclosures.

Moreover, the determination of a suitable dosage regimen, including the gradually increasing dosage regimen recited in the claims, clearly would have been a matter of routine optimization on the part of the artisan of ordinary skill, the determination of suitable treatment regimens being routinely determined in the pharmaceutical arts. Thus, absent some demonstration of an unexpected result, the claims must be considered obvious. In this regard note that the clinical trials described in the specification at pages 37-39 do not appear to present any significant data in that no clear results are presented.

Therefore, it is respectfully submitted that no unexpected result has been demonstrated on the record.

Response to Arguments

All of applicant's argument on this issue has been fully considered but is not persuasive of error. Note specifically that Reuser '045 is ambiguous as to the dosage to be administered. *See* col. 12, lines 18-23, wherein dosage is discussed, albeit in the absence of any time dimension, so it is not clear whether the dosage discussed is daily, weekly, or monthly. It cannot therefore be unequivocally stated, for the purposes of § 102(e), that Reuser '045 discloses the claimed invention. However, in view of Reuser's clear disclosure that Pomple's disease is treatable by administration of human acid α-glucosidase (*see* claims 18 and 19), it is clear that Reuser in fact suggests dosages encompassed by the claims presently under examination.

Further still, it is respectfully pointed out that Reuser discloses that infantile Pompe's disease is fatal within the first two years of life, thereby suggesting that one year of survival is not the unexpected result argued by applicant. Still further, the newly added limitations regarding measuring heart function (claim 36) and enzyme uptake (claim 37) must be

considered obvious as both of these functions were known in the art at the time of applicant's invention to be indicative of the disease state to be treated. While it is noted that the Van den Hout article demonstrates such improvements as being measurable, the treatability of the disease demonstrated in particular by the Reuser '045 patent clearly suggests such a result.

Further still, it is not clear how claim 38 differentiates from the prior art because the prior art clearly suggests administering to more than one patient, and as discussed above, discloses that the survival rate is up to two years, much longer than the six months recited in the claim. Thus, if there is some difference between the claims and the prior art in this regard, the difference does not appear to be present in the claims. The rejection must therefore be maintained.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Francisco C Prats
Primary Examiner
Art Unit 1651

FCP
December 11, 2001